DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2014 Budget Request

Statement for the Record

Senate Subcommittee on Labor-HHS-Education Appropriations

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Mr. Chairman and Members of the Subcommittee:

I am pleased to present the President's budget request for the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH). The Fiscal Year (FY) 2014 NIBIB budget request of $338,892,000 is $1.2 million more than the comparable FY 2012 level of $337,728,000. The mission of NIBIB is to improve human health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the engineering and physical sciences with the life sciences to advance basic research and medical care. As we enter our second decade as an NIH Institute, NIBIB is continuing to build on that integration.

ADVANCES IN REGENERATIVE MEDICINE

Tissue engineering and regenerative medicine utilizing stem cell advances are being developed to aid our wounded warriors and the general population. Working toward this goal is the Armed Forces Institute for Regenerative Medicine (AFIRM), which centers on NIBIB-funded researchers and includes more than thirty top U.S. universities and companies. The members comprise more than 100 of the most talented researchers across the nation who have joined AFIRM to develop advanced treatment options and accelerate delivery of regenerative medicine therapies to treat the most severely injured U.S. service members. An exciting example of just one of the many innovative projects underway is the development of bioprinting of skin for battlefield injuries. This technology uses a bioprinter that accurately delivers skin cells and biomaterials to rapidly cover large wounds, which are a major cause of morbidity and mortality in severe burn injuries in civilians and military personnel. Other efforts are focusing on the difficult repair of segments of bone and nerve that are missing following traumatic injuries.

In the general population, injury to cartilage can lead to joint pain and arthritis. One regenerative medicine project may help patients with knee injuries to successfully regenerate new, working cartilage through an innovative technique developed by NIBIB-funded researchers. The technique uses an engineered ‘biogel’ scaffold that solidifies when exposed to light, combined with a strong biological adhesive that covers the injured area and provides an environment that promotes the growth of cartilage-producing cells. The scaffold was recently tested in a small clinical trial in patients undergoing microfracture surgery, a first-line therapy for cartilage repair where holes are drilled in the cartilage to encourage new growth. Patients who received the biogel and adhesive, in addition to microfracture surgery, had improved cartilage growth, less scarring, and decreased pain at six months post-surgery, when compared to microfracture without the biogel treatment. The technique has the potential to transform the field of knee cartilage repair, which affects many people and is difficult to treat successfully. A large clinical trial using this promising technique is currently in progress.

REHABILITATION ENGINEERING TO ENABLE INDEPENDENCE

Overcoming several major barriers, researchers have now developed an implantable, compact, self-contained device for the sensing and transmission of brain activity. The device is an important step toward the development and use of brain-computer interfaces that harness the power of thought to remotely control computers, prosthetics, and other devices. The wireless device allows the user more freedom of movement. The small device is fully implanted beneath the skin much like a cochlear implant. It is capable of recording neural activity from 100 different sites and converting this neural activity into digital signals. It also transmits these digital signals to a wireless receiver located some distance outside the body. The device is recharged wirelessly. Initial tests in animals were successful at recording data from the device in real-time, using the wireless connection, for more than a year. The device may one day be used to control prosthetic arms and other devices, motorized wheelchairs, or for diagnostic monitoring in disorders such as in epilepsy, where patients currently are tethered to the bedside during assessment.

ENGINEERING ADVANCED MEDICAL SOLUTIONS

NIBIB continues to support technologies for more efficient and effective drug delivery. Key developments include the creation of nanoparticles that can deliver powerful cancer-killing medications to a tumor without inadvertently damaging surrounding healthy tissues. In addition to successfully targeting the tumor, a drug that is tethered to a nanoparticle can only reach its target if it survives in the blood, where the immune system is constantly removing foreign particles. To address this technical hurdle, researchers devised a stealth coating for nanoparticles that tricks the immune system into ignoring the particles. By disguising the nanoparticles to chemically look like ‘self’, the immune system doesn’t clear the particles, and more medication then can be delivered to their target tumors. Using this method, tumors in mice were reduced by 70% compared with tumors that were targeted with the cancer drug but without the nanoparticle and stealth coating. Based on these encouraging results, human clinical trials using stealth-coated nanoparticles to deliver anticancer drugs are currently underway. This technology might one day be used to deliver genes for gene-therapy treatment or to enhance biocompatibility and durability of larger foreign objects such as pacemakers and implants, whose function can degrade over time due to attacks by the immune system.

NIBIB also supports research that harnesses the power of magnetic resonance imaging (MRI) and molecular biology to probe disease mechanisms with molecular imaging techniques. This increases our understanding of the metabolic differences in various cancers and enables the development of precision diagnosis and treatment. For example, researchers have developed a technique using hyperpolarized carbon-13 (C-13) compounds to measure a metabolite found in prostate cancer. This technique provides a more rapid and accurate picture of the tumor's aggressiveness. In this method, by 'hyperpolarizing' the carbon isotope, investigators are able to increase the target signal by about 10,000-fold, making this carbon labeled signal much more readily detectable. The researchers developed a system for synthesizing, hyperpolarizing, and rapidly delivering carbon-13-labeled pyruvate, a natural human metabolite. The metabolic changes in the pyruvate level serve as a biomarker or indication for prostate cancer as the disease progresses and provide very useful measures of the aggressiveness of the tumor. Monitoring these changes may improve risk prediction, a critical issue in prostate cancer, where physicians are unable to determine whether the tumor is aggressive and life-threatening, or slow-growing and low-risk.

NEW USES OF ULTRASOUND FOR DIAGNOSIS AND TREATMENT

The immune system's natural killer (NK) cells are those that find and destroy foreign substances in the body. A human NK cell line, NK-92 can be used to target and destroy tumors. However, this promising strategy to use the immune system to fight tumors is not possible for use in the brain because NK cells cannot penetrate the blood brain barrier (BBB). NIBIB-funded researchers developed an experimental system using ultrasound to deliver NK-92 cells to tumors in the brain. The movement of the NK cells into the tumor was monitored with and without focused ultrasound disruption of the BBB. Using MRI, researchers found that approximately 1 NK cell for every 100 tumor cells had reached the brain when using focused ultrasound to open the BBB, compared to 1 NK cell per 1000 tumor cells when ultrasound was not used. These preclinical results suggest that the tumor-killing ability of immune natural killer cells combined with focused ultrasound has tremendous potential for targeting and destroying brain tumors.

Another new ultrasound imaging technique developed by NIBIB-supported researchers can noninvasively detect tumors and fibrosis in the liver. Typically, liver disease is diagnosed using liver biopsy, a surgical procedure that can be painful and cause complications. This new ultrasound-based technique, called Acoustic Radiation Force Impulse imaging does not produce harmful ionizing radiation and is relatively inexpensive compared with other imaging modalities. This means it can be used more frequently to track the progression of fibrosis. In contrast to a biopsy which can only examine a small discrete sample of the liver, this method examines the entire liver.

The technique uses focused, high intensity sound waves to produce “push-pulses” that generate shear within tissue. Ultrasound is then also used to monitor the tissue response. The tissue response is related to the stiffness properties and structure of the liver, and is displayed as a high resolution, qualitative image. This technique can also produce quantitative stiffness measurements based on the speed of the shear waves. These measurements are used to quantify specific levels of fibrosis that can be used to classify different stages of liver fibrosis.

Yet another advance is the use of the mechanical force of ultrasound to breakup thrombi and minimizes the damage to heart muscle during a heart attack. Researchers first demonstrated in porcine models of coronary arteries blocked by blood clots or thrombosis, that conventional ultrasound using a high "mechanical index" in conjunction with micro-bubbles and a conventional clot dissolving agent achieved greater restoration of flow in the blocked artery. Consequently there was also greater heart muscle salvaged. In an initial human study, this technique was then successfully and safely used in patients who presented at a hospital with evidence that a heart attack had begun. If the promise of these preliminary studies continues, this could be easily implemented at hospitals throughout the country as a first-line treatment to minimize damage in evolving heart attacks.

NIBIB will continue to target the unique scientific opportunities of the 21st century, which promise a new revolution in employing technology to advance health care.

Roderic I. Pettigrew, Ph.D., M.D.

Roderic I. Pettigrew, Ph.D., M.D., is the first Director of the National Institute of Biomedical Imaging and Bioengineering at the NIH. In 2013, Dr. Pettigrew also began serving as the Acting Chief Officer for Scientific Workforce Diversity. This new position at NIH was established for the coordination and oversight of NIH programs and activities designed to address the unique diversity and inclusion challenges of the biomedical research workforce.

Prior to his appointment at the NIH, he was Professor of Radiology, Medicine (Cardiology) at Emory University and Bioengineering at the Georgia Institute of Technology and Director of the Emory Center for MR Research, Emory University School of Medicine, Atlanta, Georgia.

Dr. Pettigrew is known for his pioneering work at Emory University involving four-dimensional imaging of the cardiovascular system using magnetic resonance (MRI). Dr. Pettigrew graduated cum laude from Morehouse College with a B.S. in Physics, where he was a Merrill Scholar; has an M.S. in Nuclear Science and Engineering from Rennselaer Polytechnic Institute; and a Ph.D. in Applied Radiation Physics from the Massachusetts Institute of Technology, where he was a Whitaker Harvard-MIT Health Sciences Scholar. Subsequently, he received an M.D. from the University of Miami School of Medicine in an accelerated two-year program, did an internship and residency in internal medicine at Emory University and completed a residency in nuclear medicine at the University of California, San Diego. Dr. Pettigrew then spent a year as a clinical research scientist with Picker International, the first manufacturer of MRI equipment, where he helped develop their first cardiac imaging technology. In 1985, he joined Emory as a Robert Wood Johnson Foundation Fellow with an interest in non-invasive cardiac imaging. His current research focuses on integrated imaging and predictive biomechanical modeling of coronary atherosclerotic disease.

Dr. Pettigrew's awards include membership in Phi Beta Kappa, the Bennie Award (Benjamin E. Mays) for Achievement, and being named the Most Distinguished Alumnus of the University of Miami (1990). He was the Radiological Society of North America's 75th Diamond Jubilee Eugene P. Pendergrass New Horizons Lecturer. He is also the recipient of the Herbert Nickens Award of the ABC, the Pritzker Distinguished Achievement Award of the Biomedical Engineering Society, and the Distinguished Service Award of the National Medical Association. He has been elected to membership in two components of the US National Academies: the Institute of Medicine, and the National Academy of Engineering.